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**REMARKS****STATUS OF THE CLAIMS**

Applicants respectfully request entry of the amendment to claim 20 as it places the claim in condition for allowance and/or in better position for appeal. The amendment will not require any additional searching on the part of the Examiner because Claim 26 already includes the same limitation. Claims 17-28 are pending in the present application and under examination. Claim 29 is withdrawn and claims 1-16 are canceled.

**REJECTION OF CLAIMS UNDER 35 U.S.C. § 103(a) – 3 References**

Claims 17-23 and 25-27 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Constantino *et al.* (*Vaccine* 10:691-698, 1992) and van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996).

The applicants respectfully traverse. In order to establish a *prima facie* case of obviousness, three criteria must be met: (1) the cited references must teach or suggest all elements of the claimed invention, (2) there must be a teaching or suggestion to modify or combine the references, and (3) there must be a reasonable expectation of success.

1. **No Motivation to Combine**

There is no *prima facie* case of obviousness as there is no motivation to combine. As discussed in the response submitted August 22, 2005, van der Voort *et al.* do not mention oligosaccharides from serogroup C *N. meningitidis* (NmC) conjugated to a carrier and Constantino *et al.* do not mention proteoliposomic vesicles from serogroup B of *N. meningitidis* (NmB). There can be no teaching or suggestion to combine one with the other where they do not mention anything in relation to the other. To remedy this lack, the Examiner has asserted that Paradiso *et al.* provides the motivation to combine, specifically citing to the following paragraph bridging pages 272 and 273:

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A significant portion of the morbidity from meningococcus is caused by group B. Unfortunately, the capsule from group B is not very immunogenic in people because of the similarity to saccharide structures on human cells. For this reason, and because of the potential for anti-group B antibody to cross-react with brain tissue, alternative approaches have been sought. Most of the work has been done on outer membrane vesicles prepared from cells of virulent group B strains [10]. It seems likely that in the future it will be desirable to mix such a vaccine with the group C and/or group A conjugates. Since these vesicle preparations contain an array of proteins and lipids, the combinations *will create a new set of formulation challenges* not unlike those encountered in mixing conjugate vaccines with DTP. [emphasis added]

A motivation to combine must suggest the desirability of making the combination otherwise it's not a *motivation*. Paradiso *et al.* do not cite to a reason that would motivate one of skill in the art to combine the references. Rather, Paradiso *et al.* suggest that in the future there may be some uncited reason that it would be desirable. Further, in the very next sentence, Paradiso *et al.* state that there *will* be challenges to formulation of such a combination. Therefore, Paradiso *et al.* teach that there is no motivation today, but at best there may be a motivation in the future and that those of skill in the art will face difficulties at such future time in making the combination.

## 2. No Reasonable Expectation of Success

Even if Paradiso *et al.* could be read as teaching or suggesting some reason that it would be desirable to combine the teachings of Constantino *et al.* and van der Voort *et al.*, one of skill in the art would not have a reasonable expectation of success. Support for this assertion may be found in the text of Paradiso *et al.* itself. As noted above, Paradiso *et al.* state that there *will* be challenges, not that there might be difficulties. Thus, the very reference that the Examiner has asserted to provide a motivation to combine states that there will be challenges that must be overcome, indicating that one of skill in the art would not have a reasonable expectation of success. Furthermore, Paradiso *et al.* provide data in Table 5 on page 273 comparing a multivalent vaccine with separate application of the individual vaccine components. As discussed by Paradiso *et al.* on page 273, certain of the components produced a weaker immune response in the multivalent vaccine and certain components produced a stronger immune response in the multivalent vaccine. Thus, in

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addition to stating that there will be difficulties that need to be overcome, *Paradiso et al.* also teach that there is unpredictability in combining vaccine components into a multivalent vaccine. Each fact alone would prevent one of skill in the art from having a reasonable expectation of success in combining the teachings of *Constantino et al.* and *van der Voort et al.*, but together, there certainly could not be a reasonable expectation of success until the present inventors have actually taught that the combination in fact does work as they do in the present application.

### 3. References Teach Away

Even if a *prima facie* case of obviousness has been established, a *prima facie* case may be rebutted where there is evidence of teaching away. Teaching away may come in the form of a reference criticizing, discrediting or otherwise discouraging the solution claimed. *Paradiso et al.* clearly teach away from combining the teachings of *Constantino et al.* and *van der Voort et al.* in three ways. As discussed above, *Paradiso et al.* talk of a future desirability which implies that there is no reason at present to make the combination. *Paradiso et al.* also talk of challenges that must be overcome before such combination would actually work. *Paradiso et al.* also show that the results of combining vaccines are unpredictable, which suggests that such combination may never work. All three of these teachings would discourage one of skill in the art from attempting the presently claimed invention.

### 4. References Teach Away

In addition to the above, the three cited references fail to provide all elements of claims 20 and 26-28 and therefore fail to establish a *prima facie* case of obviousness. Amended Claim 20 includes the limitation that the "NmC oligosaccharide contains 12 to about 22 repeating units" and claim 26 (and therefore dependent claims 27-28) includes the limitation that the first antigen "contains from 12 to 22 repeating units from the NmC capsular polysaccharide ..." *van der Voort et al.* do not mention oligosaccharides from serogroup C *N. meningitidis* (NmC) conjugated to a carrier at all and *Constantino et al.* do not mention oligosaccharides from serogroup C *N. meningitidis* (NmC) conjugated to a carrier where the oligosaccharides contain 12 to 22 repeating

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units. As noted by the Examiner, Constantino *et al.* mention oligosaccharides having a polymerization degree (DP) of up to 10. Paradiso *et al.* fail to remedy this lack as it only cites to Constantino *et al.* Thus, the three cited references fail to teach or suggest all elements of claims 20 and 26-28.

Applicants therefore respectfully request that the Examiner withdraw the 35 U.S.C. 103(a) rejection of claims 17-23 and 25-27 as there is no motivation to combine the references and no reasonable expectation of success for such combination, and even if there were both, Paradiso *et al.* teach away from the claimed invention by discouraging one of skill in the art from attempting the combination. In addition, the references fail to teach an element of claims 20 and 26-28.

#### **REJECTION OF CLAIMS UNDER 35 U.S.C. § 103(a) – 4 References**

Claims 24 and 28 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Constantino *et al.* (*Vaccine* 10:691-698, 1992) and van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996) as applied to claim 17 or 26 above, and in further view of Granoff (US 6,413,520).

Applicants respectfully traverse. Granoff is not available under 102(e) as prior art. MPEP § 2136.03(II)(C)(1) clearly indicates that a U.S. Patent which claims priority to an international application filed before November 29, 2000 has a critical reference date as of the earlier of the date of completion of 35 U.S.C. 371(c)(1), (2) and (4) or the filing date of the later-filed application that claimed the benefit of the international application. Granoff indicates on its face that the date of completion of 35 U.S.C. 371(c)(1), (2) and (4) was Dec. 16, 1999 (See (86) on the cover page). Since the international application PCT/US98/13080 was filed before November 29, 2000, the critical date for Granoff is Dec. 16, 1999. Since the priority date of the present application is well before Dec. 16, 1999, Granoff does not qualify as 102(e) prior art. Therefore the citable references fail to teach "a carrier comprising polylactic acids or polyglycolic acids" as claimed under 24 and 28. Therefore a *prima facie* case of obviousness has not been established.

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In addition as discussed above, the first three references fail to render the claims obvious as there is no motivation to combine the references, there is no reasonable expectation of success for such combination, and even if there were both, *Paradiso et al.* teach away from the claimed invention by discouraging one of skill in the art from attempting the combination. The three citable references also fail to teach another element of claim 28.

Applicants therefore respectfully request that the Examiner withdraw the 35 U.S.C. 103(a) rejection of claims 24 and 28 for at least the above reasons.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

Please direct all further written communications regarding this application to:

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In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 223002100100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 9, 2006

Respectfully submitted,

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